

Office Action Summary

Application No.

10/501,407

Applicant(s)

VAN BEUSECHEM ET AL.

Examiner

Scott D. Long

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/23/2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 19-25 is/are pending in the application.
- 4a) Of the above claim(s) 10, 15-17 and 19-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-14, 24 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

The examiner acknowledges receipt of Claim amendments and Applicant Remarks, filed on 23 August 2007.

Claim Status

Claim 1 has been amended. Claim 10 has been withdrawn by the applicant. Claim 18 has been cancelled by the applicant. Claims 15-17 and 19-23 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1-9, 11-14, and 24-25 are under current examination.

Priority

This application claims benefit from foreign Application No. EP/02075108.7, filed 14 January 2002 and PCT Application No. PCT/EP03/00340, filed 14 January 2003. The instant application has been granted the benefit date, 14 January 2002, from the application EP/02075108.7.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – ENABLEMENT (35 USC 112, first paragraph)

Applicant's arguments regarding the rejection of claims 5-6 and 8 under 35 USC 112, first paragraph filed 23 August 2007 have been fully considered and they are persuasive.

Therefore, the rejection of claims 5-6 and 8 under 35 USC 112, first paragraph is hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 102

Applicant's arguments (Remarks, page 8) and claim amendments, filed 23 August 2007 regarding rejection of claims 1-2, 9, and 24-25 under 35 USC 102(b) as anticipated by Fueyo et al (Oncogene. 2000. 19:2-12) and as evidenced by Nevins (Human Molecular Genetics. 2001. 10(7):699-703) have been fully considered but they are not persuasive.

The applicant argues that the newly added claim amendments are not taught by Fueyo et al. As described in previous actions, Fueyo et al. teach all the limitations of the claims prior to the amendments of 8/23/2007. In the applicant's response (Remarks, 8/23/2007, page 7), "lysis of cancer cells infected by AdE1 encoding wildtype E1A protein is equally enhanced by p53 expression as is the lysis of cells infected with AdΔ24 viruses." Since Fueyo et al. teach an adenovirus having the same structure as that claimed in the instant application, the examiner asserts that any "accelerated cell

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lysis" or "faster release of virus progeny" would be intrinsic to the recombinant adenovirus taught by Fueyo et al. Fueyo et al indicate that their adenovirus can "express a mutant E1A protein" (p.3). The "link between the Rb/E2F pathway and the p53 response" is taught by Nevin (p.700). Consequently, the p53 apoptosis pathway is restored by expression of the mutant E1A protein. Fueyo et al. teach "the replication-competent $\Delta 24$ virus is a human adenovirus 5" (p. 2). Claims 9 and 25 are directed to "a mutation in a E1A region...of the pRb-binding CR2 domain of E1A" which "comprises a deletion...amino acids 122-129 (LTCHEAGF)...of E1A." Fueyo et al, "constructed a tumor-selective adenovirus, $\Delta 24$, that carries a 24-bp deletion in the E1A region responsible for binding Rb protein." (abstract). The deletion corresponds to "amino acid residues L, T, C, H, E, A, C, and F of the E1A" (Fueyo et al., page 8). The previous actions resolved that the amino acid residues taught by Fueyo are, in fact, LTCHEAGF.

Therefore, Fueyo et al. anticipate the instant claims and the examiner hereby maintains the rejection of claims 1-2, 9, and 24-25 under 35 USC 102(b) as anticipated by Fueyo et al. as evidenced by Nevins.

Response to Arguments - Claim Rejections 35 USC § 103

Applicant's arguments (Remarks, page 9) and claim amendments, filed 23 August 2007 regarding rejection of claims 1-8, 11-14, and 24 under 35 U.S.C. 103(a) as being unpatentable over Lin et al. (Cancer Research. Oct 15, 2000. 60. p.5895-5901) in

view of Chang et al. (USPat 6,638,762) have been fully considered but they are not persuasive.

The applicant argues that the new amendments to claim 1 overcome the instant rejection because the recombinant adenovirus taught by the combination of Lin and Chang do not teach "accelerated cell lysis" or "faster release of virus progeny" by their adenoviruses comprising a gene for a restoring factor (e.g. - p53) as compared to those adenoviruses which lack the restoring factor. Fundamentally, the newly added claim limitations have not changed the structure of the recombinant adenovirus. The recombinant adenoviruses taught by Lin in view of Chang teach the all structural limitations of the instant claims (see previous actions). The newly added limitations of claim 1 are merely a description of controls that could be used to assess the potency of the claimed adenoviruses. Since a variety of possible controls could be used to assess the potency of the claimed adenoviruses, the examiner concludes that because there is a finite number of possible controls, they are obvious to one of skill in the art and common sense. While Lin and Chang may not teach the specific controls of the newly amended claim 1, they do teach the specific structural limitations of claims 1-8, 11-14, and 24 and the type of controls suggested by the newly added limitations are obvious and not an important structural limitation.

Additionally, the applicant states that "Lin is concerned with inhibiting oncogenic transformation of cells (see abstract of Lin), **not** with apoptosis" (Remarks, page 10, emphasis added by applicant). Despite the applicant's assertion, Lin et al. display their concern for assessing a restoring factor gene (p53 14/19) comprised within recombinant

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adenoviruses, writing, "Therefore, we assessed whether p53 14/19 retained key functions of the wt protein as a transcription factor. Wt p53 is known to induce cell cycle growth arrest by transcriptionally activating the *p21^{WAF-1}* gene, and **to induce apoptosis** by transcriptionally activating the *Bax* gene as well as others (56 –59). In transient transfection assays, we compared the ability of wt p53 and p53 14/19 to transcriptionally activate *p21^{WAF-1}* and *Bax* promoters." (page 5896, col.2, emphasis added by examiner).

Therefore, the examiner hereby maintains the rejection of claims 1-8, 11-14, and 24 under 35 USC 103(a) as obvious over Lin in view of Chang.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 11-14, and 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 contains the phrase, "provided in the genome thereof, with the coding sequence of at least one restoring factor" in lines 4-5. The newly amended claim 1 has made the claim unclear. Does this mean that the adenovirus has become integrated into the host genome? Or does this phrase mean that the adenoviral genome comprises the restoring factor coding

sequence? Or does the phrase mean that the genome of the target cells have received the coding sequence of the restoring factor, but not from the adenovirus? Clarification is required.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**.

The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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